PATENTS

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Paige et al.

Group Art Unit: 1639

Serial No.: 09/429,331

Examiner: Wessendorf, Teresa D.

Filed: October 28, 1999

Docket No.: 180/110/6

Confirmation No.: 5796

For: METHOD OF PREDICTING THE ABILITY OF COMPOUNDS TO MODULATE THE BIOLOGICAL ACTIVITIES OF RECEPTORS

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DECLARATION PURSUANT TO 37 C.F.R. § 1.132

Commissioner for Patents
Washington, D.C. 20231

Sir:

1. I, Donald P. McDonnell, am a co-inventor of the subject matter disclosed and claimed in the subject above captioned U.S. patent application, which upon information and belief claims priority to PCT Application No. PCT/US99/06664, filed March 26, 1999, which upon information and belief claims priority to U.S. Provisional Application No. 60/115,345, filed January 8, 1999; U.S. Provisional Application No. 60/099,656, filed September 9, 1998, and U.S. Provisional Application No. 60/082,756, filed April 23, 1998.

2. I have had the opportunity to review the Official Action mailed on August 24, 2007 from the U.S. Patent and Trademark Office for the above-referenced subject U.S. patent application.

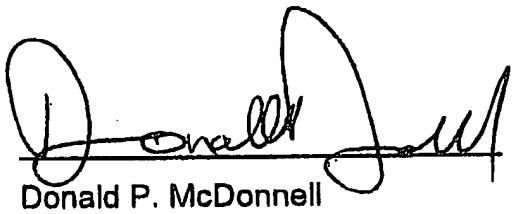
3. Attached hereto as **Exhibit A** is a true and accurate hard copy of a paper by Connor *et al.* for which I am a coauthor and senior author, and which was published in Cancer Research on April 1, 2001 (Connor *et al.*, (2001) *Cancer Research*, 61:2917-22; hereinafter "*Connor et al.*"). *Conner et al.* describes characterization of a unique conformational change induced in the estrogen receptor by the anti-estrogen compound GW5638. As described in *Connor et al.*, tumor explants that are resistant to the breast cancer therapeutic, tamoxifen, are not cross-resistant to GW5638. The results described in *Connor et al.* indicate that the lack of cross-resistance observed for GW5638 is due to the unique conformational change induced in the estrogen receptor by GW5638 that is not induced by binding of tamoxifen. The general procedures for using peptide conformational probes to determine the estrogen receptor conformational changes induced by tamoxifen and GW5638 as described in *Connor et al.* are disclosed in the subject above-referenced patent application, for example, at Examples 1-5, pages 130-159. Thus, the receptor-modulating activity of the test compound GW5638, when bound to an estrogen receptor, was predicted to be different from that of reference compound tamoxifen, according to the method of current claim 1 of the subject above-referenced patent application.

4. Attached hereto as **Exhibit B** is a true and accurate hard copy of a paper by DuSell *et al.* for which I am a coauthor and senior author, and which was published in Molecular Endocrinology in 2008 (DuSell *et al.*, (2008) *Molecular Endocrinology*, 22(1):65-77; hereinafter "*DuSell et al.*"). *DuSell et al.* describes characterization of a unique conformational change induced in the estrogen receptor by the anti-estrogen compound 27-hydroxycholiesterol (27HC). As described in *DuSell et al.*, 27HC induces a unique conformational change in both ERα and ERβ, distinguishing it from other selective estrogen receptor modulators (SERMs) whose relative agonist/antagonist activities vary in a cell- and promoter-dependent manner. The general procedures for using peptide conformational probes to determine the estrogen receptor

conformational changes induced by 27HC and other SERMs as described in *DuSell et al.* are disclosed in the subject above-referenced U.S. patent application, for example, at Examples 1-5, pages 130-159. Thus, the receptor-modulating activity of the test compound 27HC, when bound to an estrogen receptor, was predicted to be different from that of reference compound estradiol (E2), according to a method of current claim 1 of the subject above-referenced U.S. patent application.

I hereby declare that all statements herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: Feb 25, 2008

By: 

Donald P. McDonnell